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Title:

Low adherence to dietary recommendations in adult childhood cancer survivors

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Abbreviations

ACS	American Cancer Society
CCS	childhood cancer survivors
CNS	central nervous system
CVD	cardiovascular disease
FFQ	food frequency questionnaire
SCCSS	Swiss Childhood Cancer Survivor Study
SCCR	Swiss Childhood Cancer Registry
SHS	Swiss Health Survey

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ABSTRACT

Background & aims: Poor diet may increase the risk that childhood cancer survivors (CCS) will suffer from chronic disease. We compared adherence to national dietary recommendations between CCS, their siblings and the Swiss population, identified determinants of adherence, and assessed the association of adherence with cardiovascular disease (CVD) risk profiles.

Methods: As part of the Swiss Childhood Cancer Survivor Study (SCCSS), a questionnaire was sent to all Swiss resident CCS aged <21 years at diagnosis, who survived ≥5 years and were 16-45 years old at the time of the survey. We compared dietary adherence between CCS, their siblings and participants in the Swiss Health Survey (SHS), a representative survey of the general population. A multivariable logistic regression was used to assess characteristics associated with dietary adherence. We sorted CCS into four kinds of CVD risk groups based on type of treatment (anthracyclines, chest irradiation, a combination, or neither).

Results: We included 1'864 CCS, 698 siblings and 8'258 participants of the general population. Only 43% of the CCS met the recommended dietary intakes for meat, 34% for fruit, 30% for fish, 18% for dairy products, 11% for vegetables, and 7% for combined fruit and vegetables. Results were similar for both control groups. In all groups, dietary adherence was associated with gender, parental education, migration background, language region in Switzerland, smoking, alcohol consumption and sport participation. CCS with a higher CVD risk profile because of cardiotoxic treatment had no better adherence.

Conclusions: CCS have similar food patterns as their siblings and the general population, and poorly adhere to current recommendations. Awareness of the importance of a healthy diet should be raised among CCS, to prevent chronic diseases like CVD.

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1. INTRODUCTION

Cancer or the late effects of its treatment cause more than two-thirds of childhood cancer survivors (CCS) to develop chronic diseases later in life. Chronic diseases reduce quality of life, and increase morbidity and premature mortality [1, 2]. CCS are up to 15 times more likely to develop heart failure than their siblings, and almost 13 times more likely to die from circulatory diseases than their peers in the general population [1, 3]. This increased risk could be the result of cardiotoxic therapy effects due to anthracycline-containing chemotherapy and radiation therapy involving the heart. Unhealthy lifestyles, including unbalanced diets, physical inactivity and being overweight or obese, could also each significantly increase the risk of cardiovascular disease (CVD) [4].

Excess calorie intake, and consuming too little fish, fruit and vegetables are associated with higher risk of CVD in the general population. Better dietary habits may improve cardiovascular health [4, 5]. Unbalanced diet is a major modifiable risk factor for CVD, Type II diabetes, metabolic syndrome, and osteoporosis [4-7]. But a recent review that included 14 observational studies showed that childhood cancer patients and survivors in the US, Australia, Germany, Canada, and the UK rarely adhere to dietary recommendations [8]. CCS do not eat enough fruit and vegetables [9-11], dairy products [10, 11], whole grains [11, 12], or the micronutrients calcium and vitamin D [12]. They also eat too much sodium and meat [9].

Most studies that investigated dietary adherence had low sample sizes (N<500) [9-13], no control group [9, 10, 12, 14], and did not investigate the association between dietary adherence and CVD risk profiles based on received type of therapy [9, 10, 12-14]. Therefore, we analysed data from the Swiss Childhood Cancer Survivor Study (SCCSS) to (1) compare adherence to national dietary recommendations among CCS, their siblings and the general population, (2) identify socio-demographic and clinical factors associated with adherence to national dietary

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recommendations, and (3) determine if adherence to dietary recommendations in CCS differed by cardiovascular risk profiles.

2. METHODS

2.1.Sampling

2.1.1 The Swiss Childhood Cancer Survivor Study (SCCSS)

The SCCSS is a nationwide long-term follow-up study of all ≥5-year CCS registered in the Swiss Childhood Cancer Registry (SCCR), diagnosed between 1976 and 2005, and alive at the time of the study [15]. The SCCR registers children and adolescents under age 21, who are diagnosed in Switzerland with leukaemia, lymphoma, central nervous system (CNS) tumours, malignant solid tumours or Langerhans cell histiocytosis [16, 17].

From 2007 to 2012, we traced all addresses of eligible survivors for the SCCSS and sent them a long questionnaire. Non-responders were sent a second copy of the questionnaire four to six weeks later. Non-responders to the second copy were contacted by phone. We used questionnaires similar to those used in US and UK CCS studies [18, 19], but added questions about health behaviours and socio-demographic measures from the Swiss Health Survey 2007 (SHS) [20] and the Swiss Census 2000 [21]. The main domains covered by the questionnaire were quality of life, somatic health, fertility, use of current medication and health services, psychological distress, health behaviours, and socio-economic status. Detailed information on our study design was published previously [15].

The Ethics Committee of the Canton of Bern gave ethical approval to the SCCR and the SCCSS.

2.1.2 Sibling controls

From 2007 to 2012, when we sent out the questionnaire to CCS, we asked them to give us consent to contact their siblings and to provide sibling contact information. Beginning in 2010,

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we sent siblings the same questionnaire as CCS, but omitted questions about cancer history. Siblings who did not respond were sent another copy of the questionnaire four to six weeks later, but were not contacted by phone.

2.1.3 General population controls (Swiss Health Survey)

The second control group consisted of participants in the 2007 SHS survey. The SHS is a national representative telephone survey repeated every five years. The SHS compiled a randomly selected representative sample of 28'332 Swiss households with telephone land lines and attempted to contact one person per household. Of households called, 6'185 did not answer, and 3'414 refused to participate. The final sample included 18'760 participants (66% response rate) [20]. Sampling was stratified by region and conducted stepwise. Households were selected first, and then the survey was administered to anyone 15 or older who answered the phone.

2.2 Measurements

2.2.1 Dietary intake and adherence to dietary recommendations

In CCS and control groups, dietary intake was assessed with standardised open and closed questions. The same standard units and serving sizes for each food item were used in the CCS and sibling surveys. They were also the same in the SHS survey for the general population. The questionnaire to survivors and siblings offers a choice of six responses to describe frequency of intake, ranging from "never" to "several times per day". It also offers open questions where participants can indicate the portions they consume per day (**Supplemental Fig S1**). The SHS survey offers similar options, though questions about frequency of fruit and vegetable intake were phrased slightly differently. We thus transformed the SHS questions on fruit and vegetable intake into the following daily consumption frequencies: "never"=0; "less than 1/day"=0.5; "1-2/day"=1.5; "3-4/day"=3.5 and "5+/day"=5.5. From the SHS survey, we obtained fruit and vegetable consumption by summing up fresh and conserved fruit or vegetable products and fruit

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or vegetable juices. The questionnaire to CCS and siblings assessed only fruit and vegetable products. Questions about fish intake also differed slightly. In the SHS survey, the general population could indicate the exact number of days per week they consumed fish, but CCS and siblings could only select from categories that specified a range.

We used current recommendations from the Swiss Society of Nutrition (SSN) to determine adequate intake of fruit, vegetable, meat, fish, and dairy products [22]. SSN recommendations are in line with those of other European countries [23-25]. We determined failure to comply with these dietary recommendations by calculating the proportion of participants who did not eat the minimum recommended daily number of servings of each food group. The lowest values of the following recommended ranges were our cut-off values: two portions of fruit (120g) per day; three portions of vegetable (120g) per day; one portion of fish (100-120g) per week, and three portions of dairy (2dl milk, 150-200g yoghurt or 30-60g cheese) per day. We used the maximum cut-off value for meat: three portions of meat (100-120g) per week.

2.2.2 Explanatory variables from the Swiss Childhood Cancer Survivor Study (SCCSS)

We assessed the following explanatory variables from the questionnaires submitted by CCS, siblings, and the general population: socio-demographic data (gender; age at survey; education level; parents' education level; migration background; and, language region in Switzerland) and lifestyle factors (body mass index [BMI]); smoking; sport participation; and, alcohol consumption). Participants who were not Swiss citizens at birth, not born in Switzerland, or had at least one parent who was not a Swiss citizen were designated to have a migration background. We classed education into four categories, according to the Swiss Census: compulsory schooling only (≤9 years); vocational training (10-13 years); upper secondary education (higher vocational training or college); and, university degree. We divided highest education level of parents into three categories: primary schooling (compulsory schooling only [≤9 years]);

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secondary education (vocational training [10-13 years]; higher vocational training or college); and, tertiary education (university degree). We calculated BMI from self-measured height and weight, dividing weight by height in meters squared (kg/m^2). For adolescents (16–19 years at survey), we standardized BMI into z-scores for age and gender using the Swiss references [26]. BMI was classified as underweight (>19yrs: <18kg/m^2; ≤19yrs: <-2 Z-scores), normal weight (>19yrs: ≥18 - <25kg/m^2; ≤19yrs: ≥-2 - ≤1 Z-scores), overweight (>19yrs: ≥25 - <30kg/m^2; ≤19yrs: >1 - ≤2 Z-scores), and obese (>19yrs: ≥30kg/m^2; ≤19yrs: >2 Z-scores). Sport participation was classified as ‘‘sports’’ if respondents reported engaging at least somewhat intensely in a targeted gym or sport for at least one hour per week, or ‘‘no sports’’ if participation was lower.

2.2.3 Explanatory variables from the Swiss Childhood Cancer Registry (SCCR)

Clinical information was extracted from the SCCR. We recorded diagnosis and the age at which cancer was diagnosed. Diagnosis was classified according to the International Classification of Childhood Cancer – 3rd Edition [27]. Chemotherapy was divided into “anthracyclines”; “other chemotherapeutic agents” or “no chemotherapy”. Radiotherapy was classified as “chest radiotherapy” if direct radiation was applied to the chest, “other radiotherapy” or “no radiotherapy”. Chest radiotherapy included total body irradiation, mantlefield irradiation or irradiation to the thorax, mediastinum, or thoracic spine. There was a record if a CCS had relapsed during follow-up time.

2.3 Statistical Analysis

Our analysis included all participants in the SCCSS (CCS and siblings) and the SHS (general population), aged 16-45 years at time of survey. Both control groups included more women and older persons than the CCS. Migrants and non-German speakers were less frequent among siblings, but more frequent in the general population. To increase the validity of the comparison

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between CCS and the control groups, we standardised both control groups for gender, age, migration background, and language region, according to the distribution in CCS (**Table I**). Standardisation was applied in all analyses, and was used as in previous publications [28, 29].

The first step in our analysis was to compare socio-demographic and clinical characteristics and adherence to national dietary recommendations in CCS and control groups using chi^2 tests.

Second, we used logistic regressions to determine factors associated with dietary adherence by estimating crude and adjusted odds ratios (OR) and 95% confidence intervals (95%CI). In univariable analyses, we tested each individual socio-demographic and lifestyle variable. If variables were significant on a p-value of <0.05, we included them in the multivariable analyses. We performed Wald tests to calculate global p-values. We used interaction terms to formally test differences in effects of risk factors between CCS and controls. We selected potential confounders and effect modifiers based on the literature.

Third, and in CCS only, we investigated associations between adherence to dietary recommendations and different CVD risk profiles (the profiles were based on type of treatment). CVD risk profiles were categorized as “no chemo- and radiotherapy”, “other chemo- and/or radiotherapy” (no anthracyclines and no chest radiotherapy), “either anthracyclines or chest radiotherapy”, and “both anthracyclines and chest radiotherapy”. We conducted tests for linear trend for the ordered categorical CVD risk profiles.

We performed sensitivity analyses to compare standardised data for gender, age, migration background and language region in both control groups according to the distribution in CCS to non-standardised data. We used Stata software (version 14, Stata Corporation, Austin, Texas) for all statistical analysis. All statistical significance tests were two-sided with a significance level of 5%.

3. RESULTS

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3.1.Characteristics of study population

We traced and contacted 3'593 of 4'116 eligible CCS. Of those we contacted, 2'527 (70%) returned the full questionnaire. We excluded 520 participants who were younger than 16 or older than 45 years, and 143 participants who did not provide data on diet. We thus included 1'864 CCS in the analysis (**Supplemental Fig S2**). We had consent to contact 1'295 siblings, of whom 733 returned the questionnaire; 32 were outside the age range, and three did not provide data on diet. Of 28'332 households surveyed, one person per each of 18'760 households (66%) replied to the survey. Of these, 8'258 were between 16-45 years old.

More CCS than controls had completed compulsory schooling only (12% vs. 7% siblings and 5% general population) and fewer CCS had earned a university degree (7% vs. 11% siblings and 10% general population; all $p<0.001$) (**Table I**). Mean BMI did not differ between groups, but BMI categorisation was significantly different: CCS were more likely to be underweight (4% vs. 1% siblings and 2% general population) or obese (7% vs. 4% siblings; and 4% general population; $p_{siblings}=0.001$ and $p_{SHS}<0.001$). CCS were less likely to smoke than the general population (24% vs. 34%, $p_{SHS}<0.001$). We found no significant difference between CCS and siblings for smoking. More CCS than controls consumed never or rarely alcohol (51% vs. 36% siblings and 44% general population; all $p<0.001$). CCS were less likely to engage in sports than both control groups (55% vs. 65% siblings and 64% general population; all $p<0.001$).

Among CCS, the largest diagnostic group was leukaemia (32%), followed by lymphoma (20%) and CNS tumours (14%) (**Table II**). When we divided CCS into CVD risk profiles, 17% did not receive chemo- and radiotherapy (lowest risk category), 37% had received other chemotherapeutic agents than anthracyclines and/or other radiotherapy than chest radiotherapy, 39% either anthracyclines or chest radiotherapy, and 7% had both anthracyclines and chest

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radiotherapy (highest risk category). Mean age at diagnosis was 8.8 ± 5.5 years and mean time since diagnosis was 17.2 ± 6.9 years. Twelve percent had experienced a relapse.

3.2 Dietary adherence in CCS and control groups

Overall dietary adherence was low (**Fig I, Supplemental Table S1**). The highest scores on adherence were for meat (37-43%), fish (26-55%) and fruit (24-39%). The lowest scores for adherence were for the combination of two servings of fruit/day and three servings of vegetables/day (6-7%). We saw no large differences between CCS, their siblings, and the general population. CCS were slightly less adherent than their siblings to fruit intake recommendations ($p_{siblings}$=0.011), more adherent to recommendations for eating meat ($p_{siblings}$=0.011), and tended to adhere better to recommendations for eating fish ($p_{siblings}$=0.075). CCS were more adherent than the general population to recommendations for fruit (p_{SHS}<0.001), meat (p_{SHS}=0.003) or dairy products (p_{SHS}<0.001), but less adherent to recommendations for vegetables (p_{SHS}=0.009) or fish (p_{SHS}<0.001). Although these differences were statistically significant, the absolute differences between the groups were small and clinically irrelevant.

3.3 Determinants of dietary adherence in CCS and control groups

In univariable logistic regressions, factors associated with better adherence to dietary recommendations were female gender, age (depending on the food group), higher education, higher parental education, migration background, residence in the French or Italian speaking part of Switzerland, being underweight or having a healthy BMI, not a smoker, no-to-rarely alcohol consumption (those who ate enough fish tended to consume more alcohol), and sport participation (**Results available upon request**). Since all socio-demographic and lifestyle variables were significant for at least one outcome, we included all of them in the multivariable

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models when we investigated CCS (**Table III, Supplemental Table S2**), their siblings (**Results available upon request**), and the general population (**Supplemental Table S3**), and when we looked at cancer-related determinants in CCS only (**Supplemental Table S5**).

Socio-demographic and lifestyle determinants. In CCS, several socio-demographic and lifestyle factors were related to adherence to dietary recommendations in multivariable logistic regressions (**Table III, Supplemental Table S2**). CCS who ate enough fruit and vegetables were more often female, had more educated parents, a migration background, residence in the French-speaking part of Switzerland, participated in sports, and tended to have higher BMI. Meat adherence was associated with female gender, older age, a migration background, residence in the French- or Italian-speaking part of Switzerland, current smoking, never-to-rare alcohol consumption, and sports participation. As with adherence to recommendations for meat intake, CCS who ate enough fish were older; had a migration background, were from the French- or Italian-speaking part of Switzerland, and participated in sports. More highly educated participants and non-smokers were more likely to eat enough fish. The opposite was true for the intake of dairy products. Maleness, younger age, and no migration background were associated with adherence to recommendations for dairy intake.

After we performed interaction tests (**Supplemental Table S4**), we found no evidence that the effect of risk factors differed between CCS and their siblings (all interaction p-values >0.05). This means that the same socio-demographic and lifestyle factors were associated with dietary adherence in both CCS and siblings. However, the strength of the associations between some risk factors and dietary adherence differed between CCS and the general population (interaction p-values <0.05) (**Supplemental Table S4**). When comparing effect sizes between CCS (**Table III, Supplemental Table S2**) and the general population (**Supplemental Table S3**), differences were small and hardly clinically relevant.

Cancer-related determinants. After controlling for socio-demographic and lifestyle factors, we found that cancer-related factors among CCS were not significantly associated with

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adherence to dietary recommendations (**Supplemental Table S5**). CCS diagnosed at age 5-9 were less likely to adhere to combined fruit and vegetables and vegetable recommendations than CCS diagnosed younger than five years.

We found no important differences in the sensitivity analyses that compared standardised data to non-standardised data. Both types of analyses led to the same conclusions.

3.4 Dietary adherence among different CVD risk profiles

There was no relevant difference in adherence to dietary recommendations between CVD risk profiles based on type of chemo- and radiotherapy and p-values for trend were insignificant ($p>0.10$) (**Figure 2**). We did see a trend for adherence to meat recommendations, which was slightly higher in all risk groups than in the group of CCS who had not received chemo- and radiotherapy.

4. DISCUSSION

4.1 Principal findings

We found that CCS poorly adhered to dietary recommendations, but that adherence of siblings and the general Swiss population was equally poor. Predictors of adherence in CCS were similar in siblings, but differed somewhat from the general population. Adherence to dietary recommendations was not better among CCS with a higher CVD risk because of cardiotoxic treatment.

4.2 Dietary adherence in Switzerland and the rest of the world

Ours is the largest study to compare the adherence of adolescents and young adult CCS and control groups to national dietary recommendations. Our findings on low adherence are in line with data from the 6th Swiss Nutrition Report [30] and the population-based cross-sectional

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study of de Abreu et al. 2013 in the French-speaking part of Switzerland, which reported only 39% of the participants adhered to Swiss recommendations for fruit intake, 7% for vegetables, 61% for meat, 66% for fish and 8% for dairy products [31]. We found adherence for meat was lower, probably because national recommendation guidelines for consumption of meat dropped from ≤5 days per week to ≤1-3 days per week [22] between de Abreu's and our study. Our findings also concord with the few studies that reported dietary adherence among CCS. Demark-Wahnefried et al. found that only 20% of the 209 US CCS consumed the recommended five servings of fruit and vegetables per day [32]. Similar poor adherence levels for fruit and vegetables were observed in more recent and larger US studies [13, 14]. Although meat recommendations were different in previous studies, overall meat adherence was low in CCS. Only 10% adhered to the World Cancer Research Fund/American Institute for Cancer Research guidelines to consume less than 80 grams of red meat per day [14]. A study from the US CCSS also found that less than half of CCS met the American Cancer Society (ACS) recommendations to eat less than 18 oz (+/-500g) of red and processed meat per week [13].

4.3 Dietary adherence among CCS compared to control groups

CCS and siblings had similar levels of dietary adherence, as also found by a US study based on Healthy Eating Index-2005 (HEI) scores [11]. However, our comparison of CCS to the general population revealed more significant differences in adherence. When we looked at the proportion of CCS and the general population that adhered to dietary recommendations (e.g., 18% adherence for dairy products among CCS vs. 12% among the general population) we found the observed differences were, although statistically significant, clinically irrelevant. A cross-sectional study between CCS and the general US population came to similar conclusions, finding no relevant differences after basing their analyses on adherence criteria from the ACS Guidelines on nutrition [13].

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4.4 Gender and migration background differences

Females adhered better to fruit, vegetable, and meat recommendations. Males were more adherent to dairy products recommendations. These match previous Swiss [31, 33] and European [34] findings. The reasons for these gender differences are unclear. Males and females may be socialized differently, and exposed to different amounts of information about diet and health. It is also possible that males and females have different tastes, different levels of interest in healthy diets, and different eating goals. Although women were almost twice as likely to adhere to dietary recommendations for fruit, vegetable and meat intake than men were, adherence levels were still far from ideal for either gender and both need improvement.

Migration background was associated with higher adherence to recommendations for all food groups except dairy products. Much of the Swiss population with a migration background is from Southern Europe, where people commonly eat a Mediterranean diet already rich in fruit, vegetables and fish, and poor in meat and dairy products [35].

4.5 Dietary adherence and CVD risk profiles

Low intake of fruit, vegetable, fish and dairy products are already a concern in the general population, but may have a more deleterious effect on CCS. Better adherence to dietary recommendations lowers the risk of all-cause mortality, CVD mortality, cancer incidence and mortality, and Type II diabetes mellitus among adults by 15 to 22% [6]. Since CCS are up to 15 times more likely to have heart failure than their siblings [1], risk factors like poor diet may exacerbate this [4-6]. CCS with baseline risk elevated by cancer treatment may strongly benefit from a good diet, but we found no differences in adherence levels among CCS for different CVD risk profiles. As in our study, Landy et al. found little to no difference between dietary intake and cancer diagnosis and therapy, except for exposure to cranial irradiation, which was related to even poorer adherence [11].

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4.6 Implications for clinical practice

The national organisation Swiss Cancer League (www.liguecancer.ch) emphasizes in cancer prevention campaigns to increase fruit and vegetable consumption and reduce alcohol, red and processed meat intake. This could partly explain the higher levels of fruit and meat adherence in CCS. However, it is unclear to which extent CCS are aware of these dietary recommendations and if diet is perceived as a risk factor for late effects. Current CCS guidelines do not specifically focus on diet [8].

We performed a short survey among the nine Swiss paediatric oncology clinics to assess whether they discussed diet issues during follow-up visits. Six replied that they discuss diet in case CCS suffer from nutritional related late effects, and three indicated to discuss it routinely during each follow-up visit (personal communication). Given the strong evidence about diet and health in general and the increasing data for CCS, focus should be placed on the importance of good eating habits during annual long-term follow up visits. Follow-up visits are especially recommended for CCS with moderate to severe late health effects or high risk cancer treatment, a group which could benefit of dietary counselling [36].

General dietary recommendation campaigns are equally widespread between language regions within Switzerland. As regional differences in adherence are seen, campaigns should be adapted to federal state and regional level, which will not only benefit CCS but also the general population.

4.7 Strengths and limitations

Our study is limited by the fact that all available data were self-reported; so social desirability bias and subjective interpretation could have favourably biased the results. The different survey designs (questionnaire in CCS and siblings, telephone interviews in the general population) might have influenced the results. For example, respondents might list alcohol consumption more moderately in a telephone interview than a written survey. Differences in level of

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adherence to recommendations for fruit and fish intake between CCS and the general population may have been a product of differently worded survey answers. Our study was strengthened by its national coverage of the SCCSS, our large sample size, and the high response rate among CCS, which made our results representative. We had access to high quality clinical information extracted from the SCCR. The questionnaires gave us access to a wide variety of socio-demographic, and lifestyle factors. We compared adherence of CCS with both siblings (who share environmental factors with CCS) and a representative population-based study performed simultaneously in Switzerland (so we could account for different environmental factors).

5. CONCLUSION

Large-scale studies with systematic and standardised dietary assessments, such as 24h recalls and validated food frequency questionnaires would help more precisely assess nutritional intake among CCS, and determine if food intake patterns are associated with cancer diagnoses, treatments, patient characteristics, adverse somatic late effects, and survival outcomes. Finding these connections would provide incentive for CCS to eat a balanced diet because it could lessen their chance of suffering adverse late effects. Poor eating habits may predispose CCS to chronic comorbidities or increase the likelihood they will develop a secondary neoplasm [4-6, 8, 14]. More focus should be placed on improving dietary adherence during clinical follow up, especially for CCS with high CVD risk profiles.

Though no worse than their siblings or the general population, CCS adhere poorly to nutritional recommendations, and may be more susceptible to health problems caused by poor nutrition.

STATEMENT OF AUTHORSHIP

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FB conducted the statistical analyses and wrote the article; LW and CK gave support in the statistical analyses and revised critically the manuscript; All authors have critically revised and approved the final article.

CONFLICT OF INTEREST STATEMENT

The authors report no conflict of interest.

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583 **TABLES**

584 **Table I. General characteristics of childhood cancer survivors (CCS), their siblings and**

585 **the general population (Swiss Health Survey)**

	CCS (n=1864)	**Siblings[a] (n=698)**		**General population[a] (n=8258)**	
Characteristics	n (%)	n ($\%_{std}$)	***p-value***[b]	n ($\%_{std}$)	***p-value***[c]
Gender					
Male	978 (52)	288 (53)	***n.a.***	3886 (53)	***n.a.***
Female	886 (48)	410 (47)		4372 (47)	
Age at survey (years)					
<20	449 (24)	110 (24)	***n.a.***	747 (25)	***n.a.***
20-29	886 (48)	331 (48)		1959 (47)	
30-39	438 (24)	201 (23)		3246 (23)	
≥40	91 (5)	56 (5)		2306 (5)	
Education (highest degree)					
Compulsory schooling	230 (12)	45 (7)	***<0.001***	596 (5)	***<0.001***
Vocational training	872 (47)	292 (42)		4668 (63)	
Upper secondary education	632 (34)	286 (40)		1924 (22)	
University education	130 (7)	75 (11)		1070 (10)	
Parents' education (highest degree)					
Primary schooling	169 (9)	59 (7)	***0.214***	n.a.[d]	***n.a.***
Secondary education	1351 (73)	513 (73)			
Tertiary education	344 (19)	126 (20)			
Migration					
No migration background	1423 (76)	561 (77)	***n.a.***	4901 (77)	***n.a.***
Migration background	441 (24)	137 (23)		3357 (23)	
Language region of Switzerland					
German speaking	1310 (70)	565 (71)	***n.a.***	5068 (70)	***n.a.***
French speaking	495 (27)	112 (26)		2580 (27)	

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Italian speaking	59	(3)	21	(3)		610	(3)	
BMI[e]								
Underweight	72	(4)	11	(1)	***0.001***	178	(2)	***<0.001***
Normal	1324	(71)	508	(75)		5702	(76)	
Overweight	347	(19)	146	(20)		1907	(18)	
Obese	121	(7)	33	(4)		471	(4)	
Smoking								
Current smoker	443	(24)	155	(23)	***0.491***	2688	(34)	***<0.001***
Stopped smoking	210	(11)	101	(13)		1209	(10)	
Never smoked	1211	(65)	442	(64)		4361	(56)	
Alcohol								
Never/rarely	956	(51)	275	(36)	***<0.001***	3728	(44)	***<0.001***
Weekly, ≥1 std drink/week	747	(40)	358	(52)		4012	(53)	
Daily, 1 std drink/day	65	(3)	22	(3)		435	(3)	
Frequently, >1 std drink/day	96	(5)	43	(9)		83	(6)	
Sports								
Yes	1016	(55)	447	(65)	***<0.001***	4722	(64)	***<0.001***
No	848	(46)	251	(35)		3536	(36)	

BMI: body mass index; n.a.: not applicable; std: standard alcoholic drink;

[a]: Standardized on gender, age at survey, migration background and language region according to the CCS population;

[b]: p-value calculated from Chi-Square statistics comparing CCS to siblings (2-sided test);

[c]: p-value calculated from Chi-Square statistics comparing CCS to general Swiss population (2-sided test);

[d]: No data on parental education within the Swiss Health Survey available;

[e]: BMI Z-scores were calculated for subjects ≤19 years, BMI scores (kg/m^2) were calculated for adults (>19 years).

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595 **Table II. Clinical characteristics of childhood cancer survivors (CCS)**

	CCS (n=1864)	
Characteristics	n	(%)
Clinical treatment		
Paediatric cancer centre[a]	1590	(85)
Other clinic	274	(15)
ICCC3 diagnosis		
I: Leukaemia	600	(32)
II: Lymphoma	371	(20)
III: CNS tumour	261	(14)
IV: Neuroblastoma	76	(4)
V: Retinoblastoma	40	(2)
VI: Renal tumour	108	(6)
VII: Hepatic tumour	11	(1)
VIII: Bone tumour	81	(4)
IX: Soft tissue sarcoma	112	(6)
X: Germ cell tumour	89	(5)
XI & XII: Other tumour	47	(3)
Langerhans Cell Histiocytosis	68	(4)
CVD risk profile		
No chemo- and RT	314	(17)
Other chemo- and/or RT (no anthracyclines and no chest RT)[b]	694	(37)
Either anthracyclines or chest RT[c]	718	(39)
Both antracyclines and chest RT	138	(7)
Age at diagnosis (years)		
<5	604	(32)
5-9	455	(24)
10-14	521	(28)
15-20	284	(15)

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Time since diagnosis (years)		
<15	746	(40)
≥15	1118	(60)
History of relapse		
No	1636	(88)
Yes	228	(12)

CNS: central nervous system; CVD: cardiovascular disease; ICCC3: International Classification of Childhood Cancer, 3rd edition; RT: radiotherapy;

[a]: Including the following clinics with paediatric oncology units Kantonsspital Aarau AG, Universitäts-Kinderspital Basel, Ospedale S. Giovanni Bellinzona, Universitäts-Kinderklinik Bern, Hôpital des Enfants Genève, CHUV Lausanne, Kantonsspital Luzern, Ostschweizer Kinderspital St. Gallen, Universitäts-Kinderspital Zurich;

[b]: Other chemotherapeutic agents and radiotherapy than anthracyclines and chest radiotherapy;

[c]: Chest radiotherapy includes direct radiation applied to the chest, including total body irradiation, mantlefield irradiation or irradiation to the thorax, mediastinum, or thoracic spine.

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Table III. Adherence to dietary recommendations among childhood cancer survivors, and socio-demographic predictors for adherence (retrieved from multivariable logistic regressions)

	Fruit/vegetable ≥5 portions/day (n=123)			Fruit ≥2 portions/day (n=624)			Vegetable ≥3 portions/day (n=196)		
	%[a]	OR (95%CI)[b]	p-value[c]	%[a]	OR (95%CI)[b]	p-value[c]	%[a]	OR (95%CI)[b]	p-value[c]
Gender									
Male	5	1.00 (ref)	***0.051***	26	1.00 (ref)	***<0.001***	8	1.00 (ref)	***0.002***
Female	8	1.48 (1.00; 2.18)		42	2.18 (1.77; 2.69)		13	1.67 (1.21; 2.29)	
Age at survey (years)									
<20	7	1.00 (ref)	***0.512***	35	1.00 (ref)	***0.938***	11	1.00 (ref)	***0.542***
20-29	7	1.23 (0.75; 2.02)		34	1.02 (0.78; 1.34)		11	1.18 (0.79; 1.76)	
30-39	7	1.26 (0.70; 2.25)		32	0.97 (0.70; 1.33)		9	0.91 (0.56; 1.48)	
≥40	3	0.56 (0.16; 1.96)		31	0.89 (0.53; 1.50)		9	0.83 (0.36; 1.89)	
Education (highest degree)									
Compulsory schooling	9	1.44 (0.83; 2.52)	***0.138***	36	1.20 (0.87; 1.65)	***0.416***	13	1.33 (0.84; 2.10)	***0.379***
Vocational training	6	1.00 (ref)		32	1.00 (ref)		10	1.00 (ref)	
Upper secondary education	8	1.16 (0.75; 1.79)		35	1.02 (0.81; 1.29)		12	1.19 (0.83; 1.69)	
University education	3	0.39 (0.13; 1.18)		31	0.78 (0.50; 1.21)		8	0.75 (0.36; 1.58)	
Parents' education (highest degree)									
Primary schooling	6	1.00 (ref)	***0.022***	31	1.00 (ref)	***0.055***	13	1.00 (ref)	***0.141***
Secondary education	6	1.53 (0.75; 3.12)		32	1.15 (0.79; 1.67)		10	0.91 (0.54; 1.53)	
Tertiary education	9	2.64 (1.19; 5.88)		39	1.55 (1.00; 2.39)		13	1.35 (0.74; 2.46)	
Migration									
No migration background	6	1.00 (ref)	***<0.001***	32	1.00 (ref)	***0.034***	9	1.00 (ref)	***<0.001***
Migration background	10	2.07 (1.37; 3.14)		37	1.31 (1.02; 1.68)		16	1.92 (1.36; 2.70)	
Language region									
German speaking	6	1.00 (ref)	***0.423***	32	1.00 (ref)	***0.032***	10	1.00 (ref)	***0.629***
French speaking	8	1.29 (0.85; 1.95)		38	1.31 (1.04; 1.65)		12	1.13 (0.80; 1.59)	
Italian speaking	5	0.79 (0.24; 2.63)		27	0.75 (0.41; 1.37)		9	0.75 (0.29; 1.95)	
	Meat ≤1-3 days/week			**Fish ≥1 day/week**			**Dairy ≥3 portions/day**		

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	(n=807)			(n=554)			(n=330)		
Gender									
Male	29	1.00 (ref)	***<0.001***	31	1.00 (ref)	***0.616***	20	1.00 (ref)	***<0.001***
Female	59	3.09 (2.52; 3.79)		28	0.95 (0.76; 1.18)		15	0.63 (0.49; 0.82)	
Age at survey (years)									
<20	38	1.00 (ref)	***0.021***	26	1.00 (ref)	***0.001***	25	1.00 (ref)	***0.004***
20-29	45	1.41 (1.08; 1.85)		27	1.14 (0.85; 1.53)		17	0.66 (0.48; 0.90)	
30-39	45	1.62 (1.18; 2.22)		38	1.76 (1.26; 2.45)		14	0.56 (0.38; 0.83)	
≥40	45	1.58 (0.95; 2.63)		37	1.76 (1.05; 2.95)		10	0.34 (0.16; 0.72)	
Education (highest degree)									
Compulsory schooling	51	1.50 (1.09; 2.06)	***0.096***	30	1.37 (0.97; 1.93)	***0.022***	21	1.01 (0.69; 1.48)	***0.517***
Vocational training	40	1.00 (ref)		25	1.00 (ref)		19	1.00 (ref)	
Upper secondary education	45	1.10 (0.88; 1.39)		32	1.25 (0.98; 1.60)		16	0.87 (0.66; 1.16)	
University education	45	1.05 (0.68; 1.60)		48	1.77 (1.17; 2.68)		11	0.66 (0.36; 1.22)	
Parents' education (highest degree)									
Primary schooling	48	1.00 (ref)	***0.356***	37	1.00 (ref)	***0.231***	11	1.00 (ref)	***0.548***
Secondary education	42	0.98 (0.68; 1.41)		28	0.83 (0.58; 1.20)		16	1.10 (0.68; 1.78)	
Tertiary education	46	1.20 (0.78; 1.83)		35	1.03 (0.67; 1.59)		24	1.29 (0.74; 2.24)	
Migration									
No migration background	41	1.00 (ref)	***0.002***	27	1.00 (ref)	***<0.001***	19	1.00 (ref)	***0.032***
Migration background	50	1.49 (1.16; 1.90)		40	1.72 (1.34; 2.21)		15	0.70 (0.51; 0.97)	
Language region									
German speaking	42	1.00 (ref)	***0.023***	24	1.00 (ref)	***<0.001***	19	1.00 (ref)	***0.196***
French speaking	46	1.18 (0.94; 1.49)		42	1.98 (1.57; 2.49)		14	0.76 (0.57; 1.03)	
Italian speaking	59	2.08 (1.17; 3.69)		44	2.25 (1.30; 3.90)		15	0.80 (0.38; 1.68)	

607 CI: confidence interval; OR: odds ratio;

608 [a]: Column percentages are given;

609 [b]: Adjusted for: 1) socio-demographic variables: gender, age category, education level, migration
610 background, and language region in Switzerland and 2) lifestyle factors: BMI category, smoking
611 status, alcohol intake, and sport participation;

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612 [c]: global p-value for an association between adherence to national dietary recommendations and

613 the variable as a whole (Wald test comparing models with and without the variable).

FIGURES

Figure 1. Adherence to dietary recommendations among childhood cancer survivors (CCS), their siblings and the general population (Swiss Health Survey)

Data are proportions with 95% confidence intervals. Siblings and the general population (SHS) are standardised on gender, age, migration background and language region according to the CCS population. P-values were calculated from Chi-Square statistics comparing CCS to siblings or CCS to the general population (SHS) (2-sided test), *: p-value<0.05, **: p-value<0.001

Figure 2. Adherence to dietary recommendations among childhood cancer survivors over 4 cardiovascular disease risk profiles

Dots are OR's and whiskers 95% CI. CI: confidence interval; CVD: cardiovascular disease; OR: odds ratio; RT: radiotherapy not including chest. Multivariable analysis for adherence to nutritional recommendations per CVD risk profile were adjusted for: 1) socio-demographic variables: gender, age category, education level, parental education level, migration background, and language region in Switzerland and 2) lifestyle factors: BMI category, smoking status, alcohol intake, and sport participation; All p-values for trend were insignificant (p-value>0.10) between the different CVD risk profiles for adherence to dietary recommendations;

Other chemo- and/or RT indicates other chemotherapeutic agents and radiotherapy than anthracyclines and chest radiotherapy.

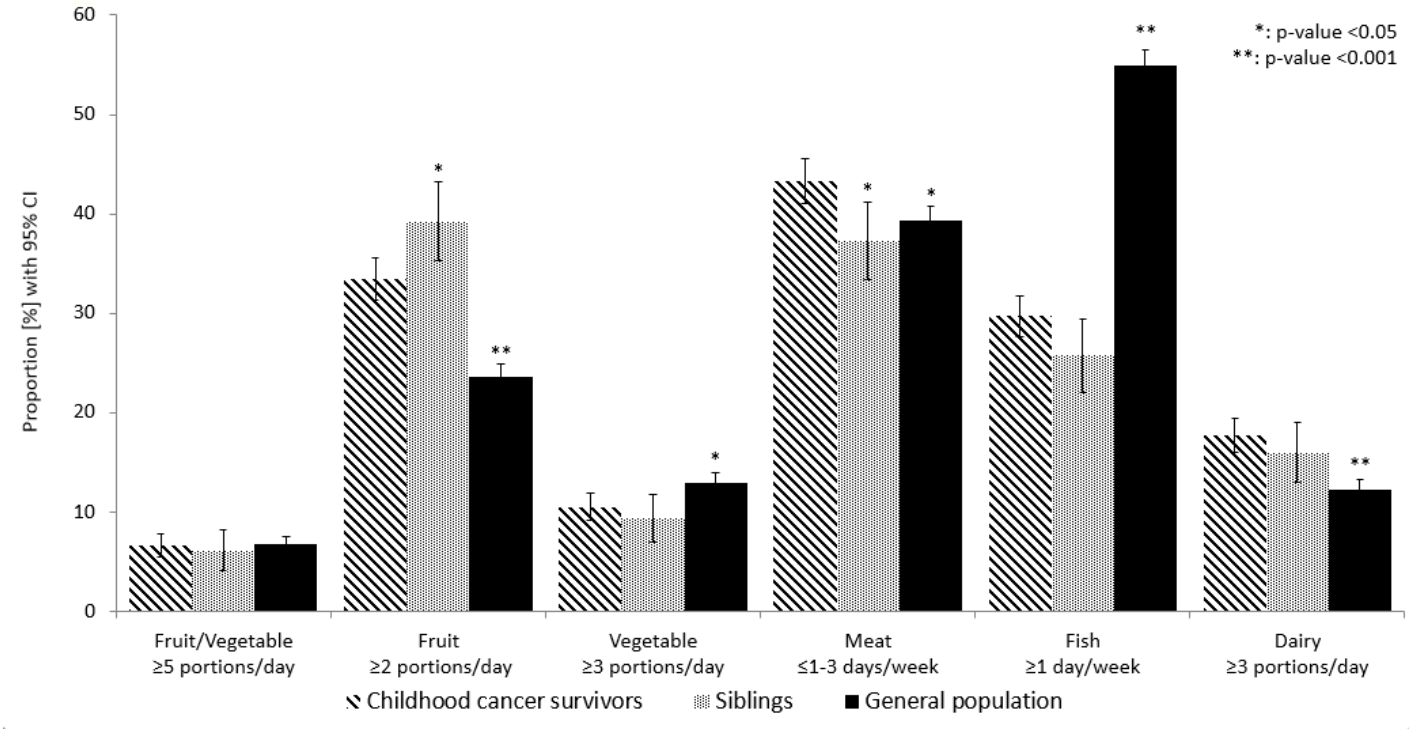
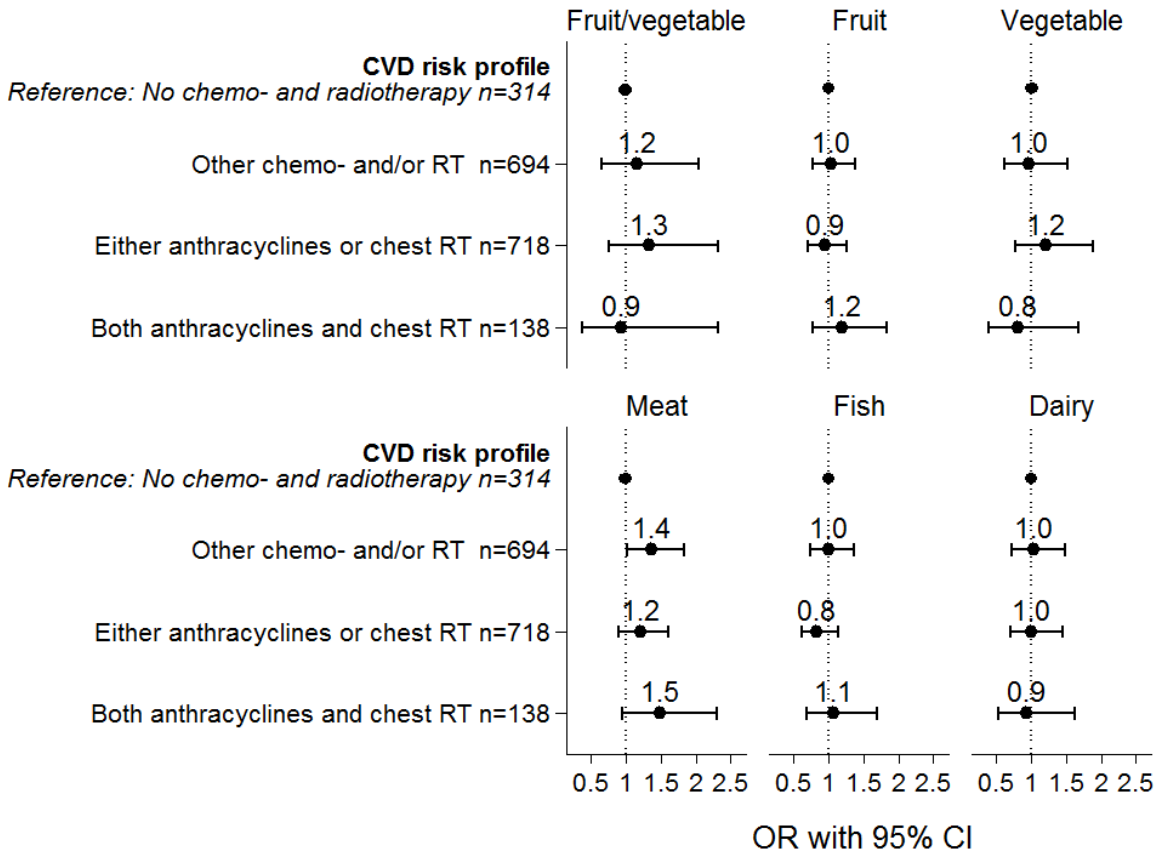

*: p-value <0.05
**: p-value <0.001
Proportion [%] with 95% CI
60
50
40
30
20
10
0
Fruit/Vegetable ≥5 portions/day
Fruit ≥2 portions/day
Vegetable ≥3 portions/day
Meat ≤1-3 days/week
Fish ≥1 day/week
Dairy ≥3 portions/day
Childhood cancer survivors
Siblings
General population

Figure 1.



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647 **Figure 2.**